

**IN THE SPECIFICATION**

Please replace the paragraph beginning at page 4, line 5, with the following  
rewritten paragraph:

Fig. 1 (SEQ ID NO:13) is a schematic drawing of a target-cleaving ribozyme  
sequence of the invention for CCR5;

Please replace the paragraph beginning at page 4, line 7, with the following  
rewritten paragraph:

Figs. 2 (SEQ ID NO:14) and 11 (SEQ ID NO:15) are schematic drawings of  
target-cleaving ribozymal DNA sequences linked to a 3'-autocatalytic sequence to  
provide a double hammerhead ribozymal DNA for targeting CCR5 and CXCR4 mRNA,  
respectively ;

Please replace the paragraph beginning at page 4, line 10, with the following  
rewritten paragraph:

Figs. 3 (SEQ ID NO:5) and 12 (SEQ ID NO:8) show the DNA sequences of  
cassettes comprising the ribozymal DNA of Figs. 2 and 11 (SEQ ID NO:14) and (SEQ  
ID NO:15), driven by a T7 promoter;

Please replace the paragraph beginning at page 4, line 12, with the following  
rewritten paragraph:

Figs. 4a (SEQ ID NO:1) and 4b (SEQ ID NO:2) are schematic drawings of target-cleaving ribozyme sequences used in this invention, in relation to CCR5 and CXCR4 mRNA targets;

### **IN THE CLAIMS**

The following claim set replaces all prior versions, and listings, of claims in the application:

1. (previously amended) A vector system comprising at least one DNA vector, the vector or vectors containing a target-cleaving hammerhead ribozymal DNA sequence under control of a promoter effective in human cells and which, upon transcription to RNA will cleave the mRNA transcribed from a target gene encoding the CCR5 or CXCR4 protein, the target-cleaving ribozymal DNA sequence, when transcribed to RNA, cleaving a target RNA sequence present in CCR5 or CXCR4 RNA, and which contains a first recognition sequence (5' to 3'):

tagattg or ctact, respectively for CCR5 and CXCR4 and downstream thereof a second recognition sequence

acttg or acgttg, respectively for CCR5 and CXCR4.

2. (original) A vector system according to Claim 1, containing target-cleaving ribozymal sequences for cleaving mRNA transcribed from both the CCR5 and CXCR4 target genes.

3. (previously mended) A vector system according to Claim 1, comprising at least two DNA vectors, wherein a first vector contains a first promoter effective in human cells, operably linked to a gene which is expressible to produce an activator protein capable of acting on a second promoter, and a second vector contains the second promoter operably linked to a target-cleaving hammerhead ribozymal DNA sequence for cleaving mRNA transcribed from the CCR5 target gene, the CXCR4 target gene or both the CCR5 and CXCR4 target genes.

4. (original) A vector system according to Claim 3, comprising at least 3 DNA vectors, wherein the second vector contains target-cleaving ribozymal DNA for cleaving mRNA transcribed from the CCR5 target gene and wherein the third vector contains target-cleaving ribozymal DNA for cleaving mRNA transcribed from the CXCR4 target gene.

5. (previously amended) A vector system according to Claim 3, wherein the second promoter is a T7 polymerase promoter and the activator protein is a T7 polymerase.

6. (currently original) A vector system according to Claim 5, wherein the T7 polymerase promoter further comprises DNA providing an internal ribosome entry site (IRES) for assisting the translation of the T7 polymerase gene in human cells.

7. (previously amended) A vector system according to claim 1 wherein the ribozymal DNA sequence further comprises, downstream of the target-cleaving ribozymal sequence, a 3'-autocatalytic hammerhead ribozymal DNA sequence. so that when the ribozymal DNA is transcribed to RNA, it has a representable form as a double hammerhead, having first and second stems of a target-cleaving ribozyme which targets CCR5 or CXCR4 mRNA and first and second stems of 3'-autocatalytic ribozyme.

8. (currently amended) A vector system according to claim 1, wherein the first and second structure-stabilising stem loops are positioned one to each side of the first recognition sequence.

9. (original) A vector system according to Claim 8, wherein a second recognition sequence is positioned downstream of the second structure-stabilising stem loop.

10. (original) A vector system acid according to Claim 9, wherein the target-cleaving ribozyme sequence comprises in order (5' to 3'):

- a first structure-stabilising stem loop;
- a first target-recognition sequence;
- a first catalytic sequence;
- a second structure-stabilising stem loop;
- a second catalytic sequence; and
- a second target-recognition sequence.

11. (cancelled).

12. (previously amended) A pharmaceutically acceptable carrier containing a vector system defined in claim 1.

13. (original) A carrier according to Claim 12 in the form of liposomes.

14. (original) A pharmaceutical composition comprising liposomes as claimed in Claim 13 and a diluent or carner.

15-16. (cancelled).

17. (previously amended) Ribozymal DNA comprising (1) a target-cleaving hammerhead ribozymal DNA sequence under control of a promoter effective in human cells and which, upon transcription to RNA will cleave the mRNA transcribed from a target gene encoding the CCR5 or CXCR4 protein, and downstream thereof (2) a 3'-autocatalytic hammerhead ribozymal DNA sequence, so that when the ribozymal DNA is transcribed to RNA, it has a form represented as a double hammerhead, having first and second steps of a target-cleaving ribozyme which targets CCR5 or CXCR4 mRNA and first and second stems of 3'-autocatalytic ribozyme, together with a common third stem joining the two hammerheads, the target-cleaving ribozymal DNA sequence, when transcribed to RNA, cleaving a target RNA sequence present in CCR5 or CXCR4 RNA, and which contains a first recognition sequence (5' to 3'):

tagattg or ctact, respectively for CCR5 and CXCR4 and downstream thereof a second recognition sequence

acttg or acgttgt, respectively for CCR5 and CXCR4.

18. (original) Ribozymal DNA which, when transcribed to RNA, will cleave a target RNA sequence present in CCR5 or CXCR4 RNA and which contains a first recognition sequence (5' to 3'):

tagattg or ctact, respectively for CCR5 and CXCR4  
and downstream thereof a second recognition sequence

acttg or acgttgt, respectively, for CCR5 and CXCR4.

19. (original) Ribozymal DNA according to Claim 18, comprising tandem CCR5 RNA- and CXCR4 RNA- cleaving sequences.

20 (new). A method of therapy against human immunodeficiency virus infection which comprises administering to a subject in need thereof an effective amount of a vector system as defined in Claim 1.

21 (new). A method of therapy against human immunodeficiency virus infection which comprises administering to a subject in need thereof an effective amount of a vector system as defined in Claim 2.